Allergy Abstracts

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From the Allergy Division of
The Jewish Hospital of Brooklyn

Volume 22, Number 6 November, 1957

Asthma and Hay Fever

Intermittent Positive Pressure-Aerosol Therapy in Pediatrics. Goddard, R. F., and Luft, U. S.: Dis. Chest **29**: 616, 1956.

Among 90 children with pulmonary diseases who were treated with intermittent positive pressure breathing (IPPB) there were 46 with asthma. In the handling of these children, therapeutic measures in addition to pulmonary function tests and IPPB included psychotherapy, allergic investigations, and appropriate hyposensitization, drugs, hormones (steroids), expectorants, etc. All positive pressure therapy in older children was given via the Bennett flow sensitive pressure breathing therapy unit, and in younger children via the Bennett infant pressure breathing therapy unit. In each case, Isuprel or Vaponephrin was used and, where indicated, other aerosols, such as Terramycin, Alevaire, or Tryptar were added. In this series of 46 asthmatic children whose ages varied from 1 to 17 years, therapy was started with 1 to 2 treatments daily, followed by treatments 2 to 3 times a week, then weekly treatments until improvement warranted discontinuance. Under this regime, 96 per cent of the

patients showed improvement, both subjectively and objectively, as judged by their general condition, freedom from asthma, and improvement in pulmonary function tests. "In childhood asthma, not only has IPPB provided relief and control of symptoms and arrested the progress of disease, but it has reversed the chronic changes due to edema, bronchospasm and emphysema, and promoted the restoration of normal lung compliance and elasticity." E. W.

Otorhinology and Ophthalmology

Use of Pyrrobutamine in Treatment of Rauwolfia-Induced Nasal Congestion. Conner, P. K., Jr., Kinard, S. A., Ford, R., McConn, R. G., and Moyer, J. H.: Geriatrics **12**: 185, 1957.

About two-thirds of hypertensive patients treated with Rauwolfia preparations complain of mild to severe nasal congestion. Forty-one such patients were treated with pyrrobutamine (Pyronil) while under hypotensive therapy. Six patients were given two courses of therapy for a total of forty-seven therapeutic trials. Pyrrobutamine was found to be effective in 60 per cent of the therapeutic trials, affording excellent relief in 27 per cent and partial relief in 33 per cent. The patients who obtained the most relief were usually those with mild nasal congestion or those who showed a relationship between blood pressure fall and nasal congestion. Since nasal congestion tends eventually to lessen spontaneously with prolonged administration of Rauwolfia drugs, antihistamines are offered as possible aids in tiding the patient over the early periods of nasal congestion. Sedation was found to be the most common side effect of the antihistamine treatment, but it was never severe. J. S.

Miscellaneous Allergies

Löffler's Endocarditis Parietalis Fibroplastica With Eosinophilia. Wiener, M. J., and Knights, E. M., Jr.: Am. Heart J. **53**: 157, 1957.

A 45-year-old Negro with a chronic cough of one year's duration was hospitalized. On physical examination, an edematous nasal mucosa, a rough systolic precordial murmur, a normal-sized heart, and enlarged lymph nodes were found. The white blood count was 22,100 with 70 per cent eosinophils and on occasion rose to 41,000 with 91 per cent eosinophils. Dyspnea was paroxysmal and was preceded by bouts of sneezing. A Thorne test was negative for adrenal insufficiency. A complete allergic work-up was reported as negative. The patient developed heart failure and pneumonia. The latter was accompanied by a fall in the total white and eosinophil counts. Late in the disease, cortisone was administered, but it was discontinued ten days later when ascites developed. Necropsy revealed the picture of cardiac failure. Thromboses in the right cardiac atrium and ventricle, mural thrombi in the left atrium, and a firm nodule near the free margin of the mitral valve were found. Microscopically, subendocardial fibrosis, diffuse endocarditis, and mural thrombus formation were seen. There were no Aschoff nodules and no evidences of periarteritis nodosa. Parasitic infestation was ruled out. It is suggested that the etiology in this case was allergic and that this disease entity should be classified among the diffuse collagen diseases. E. K.

Experimental Histamine Headache. Von Reis, G., Lund, F., and Sahlgren, E.: Acta med. scandinav. **157**: 6, 1957.

Four normal adults and 10 patients with recurrent attacks of headache were injected intravenously with from 0.05 to 0.1 mg. of histamine. A continuous record was made of the temporal artery pulsations. Blood pressure readings

were taken frequently and symptoms were timed carefully. Facial flush, the lower limits of systolic and diastolic pressure, maximal temporal artery pulsation, and the lowest amplitude in the dicrotic notch were noted at 20 to 30 seconds after injection. Throbbing in the head was noted at 30 to 45 seconds after injection. Headache started 60 to 70 seconds after injection, while the blood pressure was rising above its resting level and the temporal artery pulsations were returning to normal. "In no instance" was it found "that headache occurred during the phase of vasodilation." It is concluded that headache occurs when the physical changes due to vasodilation are subsiding. E. K.

Studies on the Shape of the Temporal Artery Pulsations in Vascular Headache, Particularly Migraine. Lund, F.: Acta med. scandinav. **158**: 21, 1957.

The shape of the temporal artery pulse in two patients during the scotoma phase of migraine is described. A comparison is made with the shape of this pulse wave in experimental histamine headache. In patients experiencing scotomata there was "decreased amplitude of the pulse wave, deviation of the upper part of the ascending limb, upward displacement of the dicrotic notch, convexity of the descending limb, and prominent secondary waves," changes which are consistent with vasoconstriction. These changes occurred only on the involved side of the head and returned to normalcy with the administration of the vasodilator, Roniacol, which also served to abort the migraine attack. It is suggested that this drug may act by decreasing peripheral resistance distal to the larger extracranial arteries, thereby decreasing their distention. Temporal artery pulse wave changes following histamine injection showed "increase in the amplitude of the pulse wave, obliteration of the predicrotic wave, downward displacement of the dicrotic notch, marked concavity of the descending limb and no secondary waves." E. K.

Clinical Observations on Allergic Reactions After Penicillin With Sensitivity Tests to Penicillin and Trichophytin. Eitan, S.: Harefuah **52**: 204, 1957.

Thirty-five patients who experienced reactions after the administration of penicillin were studied. The reactions included different forms of urticaria in 29 cases, dermatitis in 3, transient ECG changes in one, urticaria with sensitivity to light in one, and fatal anaphylactic shock in one. Analysis of the case histories revealed that 25 patients had been exposed to penicillin in the past without ill effect. Ten had a past history of allergic disease and 15 had a positive allergic family history. Nine of the group had active fungus skin infections and 4 had had fungus infections in the past.

Follow-up studies were made on 23 patients, all of whom showed negative patch and scratch reactions to penicillin. Seven showed positive reactions when tested with penicillin intracutaneously (immediate, delayed, or both) and 6 reacted positively when tested intracutaneously with trychophytin (immediate, delayed, or both). Five of the latter had active fungus infection. I. G.

Dermatitis Medicamentosa Due to Antipyrine. A Study of Twenty-Eight Cases in Negroes Following the Use of a Proprietary Medication (666 Cold Preparation). Kennedy, C. B., Davis, F. H., Henington, V. M., and Sternberg, M. J.: Arch. Dermat. **75**: 826, 1957.

The authors reviewed 28 cases of dermatitis medicamentosa caused by 666 Cold Preparation. These patients had been hospitalized on a dermatological service between 1949 and 1956. All of the patients were Negroes from 21 to

64 years of age, most of them past 40. Most patients complained of a generalized pruritus and burning of the mouth and throat, with choking sensations. The rash involved the mucous membranes of the eyes, mouth, and genitals. Numerous large, pigmented bullous lesions were present, especially on the neck, trunk, thighs, and genitals. The patients were acutely ill with high temperatures. Symptoms often lasted a month, regardless of the measures employed. Patients who had had previous reactions reported an increase in severity and more rapid appearance with each recurrence.

Patch testing over areas previously involved with the rash showed positive reactions to antipyrine in 4 out of 5 cases. Tests in these areas with acetanilid, aminopyrine, acetophenetidin, acetylsalicylic acid, phenylbutazone, and phenolphthalein gave negative reactions. Reactions to tests with antipyrine in previously uninvolved areas were uniformly negative. Biopsies from fixed eruption sites showed chronic nonspecific dermatitis consistent with a fixed drug eruption. R. W.

A New Intradermal Antigen for the Diagnosis of Schistosomiasis. Sherif, A. F.: Ann. Trop. Med. **50**: 105, 1956.

A new antigen was prepared from the ova of *Schistosoma haematobium* and *Schistosoma mansoni* for the diagnosis of schistosomiasis. The method of collecting the ova, the hatching of live miracidia from the ova, and the preparation of the antigen from the killed miracidia is described. Various groups of patients were skin-tested intracutaneously with this antigen. Of 470 patients known to have active schistosomiasis, all gave positive skin reactions. Among 250 individuals who had never had schistosomiasis or any other parasitic disease, none gave negative reactions. Some of the members of this group were suffering from allergic conditions, including bronchial asthma, eczema, and urticaria. Among 224 patients who were free from schistosomiasis but were infested with other intestinal parasites, all gave negative skin reactions. In a group of 206 schistosomiasis patients who had completed a full course of antischistosomal treatment, those tested within 3 months of the completion of the treatment still showed positive reactions. After 3 months the tests tended to show negative reactions. The reading and interpretation of the reactions are discussed. It is suggested that a specific and reliable method for the accurate diagnosis of schistosomiasis has been evolved to replace the laborious and time-consuming search for schistosome ova. J. S.

Allergic Granuloma Involving the Nervous System. Noble, A., and McLetchie, N. G. B.: Canad. M. A. J. **76**: 211, 1957.

A 32-year-old man with a history of asthma since childhood developed a carbuncle, which was incised. He was given sulfonamide therapy. After ten days the patient presented symptoms which suggested acute poliomyelitis and included backache, malaise, fever, weakness, and numbness of the legs. Following admission to the hospital, he developed a typical transverse myelitis with loss of power of his legs and loss of bladder and bowel control. He showed weakness of all his muscles. His asthma became acute. Two large painful swellings developed, one on the left buttock and one on the posterior thoracic wall. They were incised and slowly healed after several months. A biopsy of the swelling on the chest wall showed acute collagen disease. The patient improved rapidly following cortisone therapy, except for the spinal cord lesion which remained unchanged even after cortisone was continued for several months. Further study ruled out an intrathecal lesion. Since the cord lesion

had come on as abruptly as the subcutaneous lesions, and since the latter were proved to be allergic granulomas, it was concluded that the same type of lesion was also present in the spinal cord. R. W.

Allergic Encephalitis. McLetchie, N. G. B., and Stevenson, W. D.: Canad. M. A. J. **76**: 208, 1957.

The authors describe two cases of allergic encephalitis. The first patient, a 40-year-old woman, was being successfully treated for tuberculosis with streptomycin, PAS, and isoniazid. After 10 months of therapy, she developed blurring of vision following an injection of streptomycin. Neurological examination at this time was essentially negative, except for a left homonymous hemianopsia. The cerebrospinal fluid pressure and all of the spinal fluid tests were normal, but the electroencephalogram showed a gross disturbance of parieto-occipital rhythms on both sides. Ventriculography and x-ray examination presented negative findings. An aspiration biopsy taken from the right parieto-occipital region showed abundant granular corpuscles and neutrophils with perivascular softening and leukocytic infiltration. On the basis of the biopsy, a tentative diagnosis of allergic encephalitis secondary to antitubercular drug therapy was made. The patient died on the twenty-second hospital day. At post-mortem examination, hemorrhagic softening, 3 cm. in diameter, was found in the right occipital lobe and smaller lesions were present in the left occipital and frontal lobes. The entire brain showed intense vascular engorgement and marked fibrin infiltration of the vessel walls.

The second patient was a 21-year-old man who was hospitalized because of repeated grand mal convulsions over a two-month period. The findings of routine laboratory tests were normal. Pneumoencephalography showed a spinal fluid pressure of 450 mm. of water. All the other spinal fluid readings were normal. Ventriculography indicated that the brain was swollen and bulging on both sides; skull x-rays showed a slight ventricular shift to the left side. A needle aspiration from the right hemisphere indicated that the tissue here was extremely soft. Microscopy revealed a universal vasculitis with marked round-cell infiltration. The endothelial cells were found to be swollen, proliferative, and pyknotic. The affected vessels were surrounded either by a cuff of round cells and leukocytes or by a zone of boggy ground substance. On the basis of these findings, a diagnosis of allergic encephalitis was made and the patient was given anticonvulsive drugs and cortisone. During the next six weeks he made a complete recovery. R. W.

Death Following Anaphylactic Reaction to Penicillin. Stern, J.: Harefuah **52**: 209, 1957.

Four fatalities resulting from the administration of penicillin since 1955 are described. They are believed to be the first such cases reported in Israel. Preventive measures are discussed. I. G.

Anaphylaxis

Inhibition of the Anaphylactic Reaction. Mongar, J. L., and Schild, H. O.: J. Physiol. **135**: 301, 1957.

Guinea pigs were sensitized to egg white by subcutaneous and intraperitoneal injections. From 3 to 16 weeks later the spleens, lungs, and uteri of the animals were removed. The tissues were chopped into minute pieces and incubated for 15 minutes with varying concentrations of different anaphylactic inhibitors. They were then incubated for 15 minutes with a solution of egg

albumin containing 2 mg. per milliliter. The solution was removed from the tissue particles by means of filter pipettes. The amount of histamine released was measured by assay on atropinized guinea pig ileum. When inhibitors were not added to the tissues, the amount of histamine released by antigen in 15 minutes varied between 6 and 60 per cent of the tissue content. If tests were made within 12 weeks after sensitization of the animal, the histamine release was usually above 20 per cent.

The effects of different inhibitors on the release of histamine were investigated. When iodoacetate was added to the tissue suspension the subsequent histamine released by antigen was greatly diminished, but the amount released was increased when compound 48/80 was added. With P-chloromercuribenzoate the anaphylactic histamine release was reduced to 49 per cent of the control. When tissues were exposed to nitrogen (creating oxygen lack) the average amount of histamine release was only 32 per cent of the control value. Cyanide produced a marked reduction of histamine release in anaphylaxis, but doubled the amount of histamine released by acetylamine. Fluoride and 2:4 dinitrophenol did not influence histamine release.

Antipyretics, such as phenylbutazone, amidopyrine, cinchophen, and antipyrine, inhibited the release of histamine by antigen from sensitized guinea pig lung. Phenol also produced marked inhibition but did not affect the release of histamine by acetylamine or compound 48/80. A small concentration of phenol in Tyrode's solution diminished the responsiveness of ileum to histamine so that the inhibitory effects of phenol on the anaphylactic contraction appeared to be due not only to a diminished histamine release, but also to a reduced response to histamine. The phenol did not denature the antibody or interfere with the antigen-antibody reaction. Substances which inhibited histamine release in anaphylaxis also inhibited oxygen consumption and muscular contractility.

The authors suggest that the antigen-antibody reaction activates a short-lived enzyme system which is necessary for the completion of the anaphylactic reaction. The mode of action of the enzyme system is unknown. Its effects are inhibited by phenol. The manner of histamine release in anaphylaxis is not the same as when it is released by organic bases. It is suggested that chemical liberators act by a physical mechanism and the antigen by an enzymatic process. The fact that dinitrophenol abolished muscular contactility in amounts which did not inhibit histamine release suggests that contraction of muscle is not essential in the process of histamine release by antigen. The high activity of the sulfhydryl inhibitors, iodoacetate and parachloromercuribenzoate, indicates that some reaction which involves free sulfhydral groups may be an important part of the anaphylactic reaction. R.W.

Production of Peptone Shock in Mice Following Administration of H. Pertussis Vaccine. Hunder, G., and Spink, W. W.: Proc. Soc. Exper. Biol. & Med. **95**: 55, 1957.

The mice populations (ABC and Swiss-Webster strains) employed in this study were resistant to doses of peptone up to 150 mg. Such doses became lethal when the mice were given 0.2 ml. of pertussis vaccine 6 days prior to the administration of the peptone. Death occurred within from one-half to 24 hours. Mice receiving Benadryl from 3½ hours before to 3 hours after the injections of peptone did not succumb. Chlorpromazine and cortisone also protected the vaccine-treated mice against the peptone.

Pertussis vaccine increases the susceptibility of mice to histamine, as well as to peptone, by a mechanism which is not understood. While this evidence suggests that histamine is liberated in the susceptible mice as a result of the

peptone administration, this hypothesis needs more conclusive proof than has been afforded to date. It is probable that histamine is not the only factor involved. B. S.

Further Studies on Release of Serotonin and Histamine During Anaphylaxis in the Rabbit. Waslkes, T. P., Weissbach, H., Bozicevich, J., and Udenfried, S.: Proc. Soc. Exper. Biol. & Med. **95**: 479, 1957.

Anaphylaxis in the rabbit is followed by elevated plasma levels of both serotonin and histamine. The present study was carried out to determine the sources of these substances by using reserpine in sensitized rabbits to deplete platelet serotonin and histamine prior to the anaphylactic reaction.

Rabbits sensitized to horse serum were given a single intravenous injection of reserpine 19 hours prior to injection of the shocking dose of antigen. After anaphylaxis, quantitative determinations were made of histamine and serotonin in the plasma, whole blood, and tissues of sensitized and control animals. The results indicated that reserpine injected into rabbits in the amount of 0.1 mg. per kilogram causes a marked lowering of platelet serotonin and histamine without reducing these substances in the intestinal tissues below the normal range. Pretreatment of sensitized rabbits with either 0.1 mg. per kilogram or 5 mg. per kilogram of reserpine causes an elevated plasma level of histamine but not of serotonin during anaphylaxis. These findings suggest that the major portion of the rise in the plasma serotonin during anaphylaxis is due to a release from platelets, whereas the plasma histamine is probably released from both platelets and tissues. This experiment has not proved that a significant amount of serotonin is released from tissues, since considerable quantities of serotonin may be released by the tissues without any apparent rise in the levels of plasma serotonin. T. Chao.

Pharmacology, Physiology, and Pathology

Antibody Protein Synthesis by Lymph Nodes Homotransplanted to a Hypogammaglobulinemic Adult. Martin, C. M., Waite, J. B., and McCullough, N. B.: J. Clin. Invest. **36**: 405, 1957.

Lymph nodes were transplanted from a tuberculin-sensitive donor into a hypogammaglobulinemic patient who was tuberculin unresponsive. The recipient was maintained on a constant dose of gamma globulin and sulfonamides and showed a constant titer of 1:10 (exogenous) typhoid H-agglutinins. Following transplantation, the recipient was given three spaced injections of typhoid vaccine.

A strongly positive tuberculin reaction was present in the recipient, when tested 2 days after transplantation. This reactivity was maximal from the 68th to the 149th day and somewhat lower between the 149th and 217th days. It was not affected by splenectomy on the 257th day. It has since persisted for "a prolonged period." Hence, the capacity to develop fixed tissue antibody is not always impaired in patients with acquired hypogammaglobulinemia.

Typhoid vaccine elicited an antibody response to both H and O antigens. A booster dose on the 98th day after transplantation resulted in an additional response. A challenge on the 168th day failed to elicit any response. The typhoid antibody titer fell off from this point, as it would for passively administered antibody. Biopsy of the recipient's own lymph nodes taken before and after the transplantation showed no change and no antibody formation. Biopsy of a transplanted node on the 19th day showed the presence of antibody for typhoid and evidence of an initial "take" of the node.

The survival time of the lymph nodes in this patient with acquired hypogammaglobulinemia is estimated at 100 to 110 days for full activity and 50 to 60 additional days for partial activity. A delayed cutaneous hypersensitivity to leukocytes of the donor was related to the time of death of the transfused nodes. No circulating agglutinins to these leukocytes could be found, thus underlining the importance of fixed tissue antibody as the mechanism for rejection of homografts. The rate of synthesis of specific antibody protein by the transplanted lymphoid tissue was estimated "at a rate comparable with that at which endocrine and exocrine tissues synthesize such unvarying protein products as enzymes and hormones." E. K.

Antibody Production After Certain Forms of Trauma. Malt, R. A., and Cope, O.: Surgery **39**: 959, 1956.

The effect of trauma on antibody production was studied because of conflicting reports in the literature regarding this matter. Rabbits were injected with known doses of radio-iodinated bovine gamma globulin and subjected to various forms of trauma, such as wounds, exposure to cold, bone fracture, and burns. The disappearance rate of the radio-iodinated bovine gamma globulin was taken as a measure of antibody production. The rabbits subjected to trauma in the form of wounds, cold, and burns handled the injected antigen in the same manner as the nontraumatized control group. Apparently this type of trauma had no demonstrable effect on antibody production. However, the group of animals subjected to bone fracture showed a significantly greater antibody response, and an explanation for this unexpected finding is offered. The susceptibility of the burned patient to infection cannot be explained on the basis of impaired antibody production. Other possible mechanisms are suggested. J. S.

Histamine Toxicity in Mice and Rats Following Treatment With Histaminase Inhibitors. Angelakos, E. T., and Loew, E. R.: J. Pharmacol. & Exper. Therap. **119**: 444, 1957.

The theory that histaminase might be important in inactivating histamine in rats and mice, species known to be resistant to histamine, was the subject of investigation. Substances known to potentiate histamine toxicity or to inhibit monoamine or diamine oxidases were tested to discover whether they produced any major effect on histamine mortality rates in these animals. Known in vitro histaminase inhibitors were included. "With the exception of imidazole, none of the compounds tested produced any major potentiation of histamine toxicity in either species." It is concluded either "that histaminase plays no major role in the insensitivity of mice or rats to histamine, or that none of the compounds tested (with the possible exception of imidazole) was a sufficiently strong inhibitor to compete successfully with large doses of histamine *in vivo*." E. K.

Comparative Hyperfibrinogenaemic Action of D- and L-Adrenaline. Mandelbaum, F., Henriques, O. B., and Henriques, S. B.: Nature **178**: 363, 1956.

Two groups of rats received 0.03 and 0.06 mg. of L-adrenaline subcutaneously per 100 Gm. body weight, respectively. Two other groups received 1 and 2 mg. D-adrenaline, respectively. Twenty-four hours later the rats were bled from the aorta and fibrinogen determinations were made. The results indicated that the dextro-compound had 2.8 per cent of the activity of the levo compound. I. G.

Immunology

Comparison of Antibody Responses Associated With the Transfer of Rabbit Lymph-Node, Peritoneal Exudate, and Thymus Cells. Dixon, F. J., Weigle, W. O., and Roberts, J. C.: J. Immunol. **78**: 56, 1957.

Accurately definable cell populations were compared as to their ability to transfer antibody synthesis to recipient animals. Donor albino rabbits were immunized over a period of one month with 250 mg. of bovine serum albumin (BSA). The transfer cells were obtained from peritoneal exudate (71 per cent macrophages) secondary to the instillation of mineral oil, from mesenteric and popliteal lymph nodes (90 per cent lymphocytes), and from thymus (97 per cent lymphocytes). Total and differential cell counts and viability determinations were made. From 10 to 20 c.c. of the suspensions were injected into recipient albino rabbits which had been given from 400 to 500 r of whole body radiation to inhibit their immune mechanisms.

Both lymph node and peritoneal exudate cell suspensions produced sizable and approximately equivalent secondary antibody responses in the recipient x-radiated animals. With comparable numbers of cells, the rate of elimination of antigen from the circulation was also similar for the two groups. Minor cell types in each group apparently were not of primary importance in the antibody response. For example, small amounts of lymph-node cells, which in number were twice the quantity of lymphocytes present in the peritoneal exudate, produced delayed or incomplete antigen elimination.

Peritoneal exudate cells and lymph-node cells, which were subjected to 200 to 500 r of x-radiation in vitro before injection into x-radiated recipients, produced similar antibody responses. However, when x-radiated cells were injected into normal, non-x-radiated rabbits, the lymph-node cells produced a better antibody response than the peritoneal cells.

In spite of obvious differences in morphology, the peritoneal exudate cells and lymph-node cells produced remarkably similar antibody responses. The two groups were comparable in their induction periods, duration of response, amounts of circulating antibody, and immunochemical behavior. Thymus cells, even in much greater numbers, produced delayed and inferior reactions.

H. Stryker.

Transfer of Lymph Node Cells to Recipient Rabbits Pre-injected With Blood Leucocytes of Donors. Harris, T. N., Harris, S., and Farber, M. B.: Proc. Soc. Exper. Biol. & Med. **95**: 26, 1957.

In previous experiments agglutinin formation had been demonstrated in irradiated rabbits following the injection of rabbit donor lymph node cells, incubated in vitro with soluble *Shigella paradysenteriae* antigen. The authors now sought to determine the effect of pretreatment of recipient rabbits with the donor's leucocytes and erythrocytes and with the leucocytes of other species. The study was prompted by the work of Medawar who had shown that, in the case of skin homografts, a second skin graft involving the same donor and recipient was more promptly rejected than the first.

Blood leucocytes totaling about 10 million, which were obtained from normal rabbit donors, were injected intradermally in 6 to 8 sites on the backs of recipient rabbits. After intervals of from one to 11 days, the recipient rabbits were irradiated and on the following day were injected intravenously with Shigella-treated leucocytes of the donor. It was found that pretreatment with leucocytes from 4 to 11 days before antigen-treated cell transfers resulted in a pronounced impairment in agglutinin formation. This effect was less apparent when the pretreatment interval was 2 or 3 days and was absent after a one-day

interval. Pretreatment with leucocytes from peritoneal exudates of the donor were as effective as blood leucocytes in preventing antibody formation. Erythrocytes had no pretreatment effect for rabbit antigen-treated cells, nor did leucocytes obtained from the chicken, cow, and horse. Pretreatment with human leucocytes tended to prevent antibody formation in more than half of the recipients, pointing to some antigenic similarity existing between human and rabbit leucocytes. The pretreatment effects of leucocytic injections are compared with those observed by Medawar following initial tissue homografts. The effects in both circumstances appear to be specific. B. S.

Effect of H. Pertussis on Sensitivity of Mice to Serotonin. Munoz, J.: Proc. Soc. Exper. Biol. & Med. **95**: 328, 1957.

Some strains of white mice fail to show increased susceptibility to histamine after pertussis injection, even though they become more vulnerable to anaphylaxis. Moreover, when both susceptibilities are present in the same animal, the anaphylactic sensitivity may outlast the histamine sensitivity by a considerable period. Therefore, the explanation for increased anaphylactic sensitivity does not depend primarily on increased susceptibility to histamine. Because serotonin behaves like histamine in many respects, its role in the increased susceptibility of pertussis-vaccinated mice was studied.

Two strains of mice which differed in their susceptibility to histamine following pertussis inoculation behaved alike in their serotonin responses under the same circumstances. They both became from 20 to 30 times more sensitive to serotonin after preparation with pertussis. The increase in sensitivity to serotonin appeared the day after the pertussis injection and reached its maximum by the third day. It persisted for as long as the twenty-fifth day. Other bacterial suspensions could not produce the increased sensitivity to serotonin which followed pertussis treatment. B. S.

Sensitivity of Pertussis-Inoculated Mice to Serotonin. Kind, L. S.: Proc. Soc. Exper. Biol. & Med. **95**: 200, 1957.

Treatment with pertussis vaccine renders mice more susceptible to histamine and to active and passive anaphylaxis. The uteri of normal and egg-white-sensitized mice are 1,000 times more sensitive to serotonin than to histamine. In these experiments, the sensitivity of pertussis-inoculated mice to serotonin was determined. In one strain of mice the LD_{50} of serotonin in pertussis-treated animals was 12.6 mg. per kilogram, as compared to 602 mg. per kilogram in uninoculated controls. In another strain, the corresponding readings were 7.9 mg. per kilogram and 364 mg. per kilogram, respectively. The susceptibility of pertussis-inoculated mice is selective. These animals are not more susceptible than normal animals to epinephrine, heat stress, methacholine, and carbaminoylcholine. B. S.

Direct and Indirect Effects of X-radiation on Antibody-Producing Cells. Dixon, F. J., Roberts, J. C., and Weigle, W. O.: J. Exper. Med. **105**: 417, 1957.

Rabbits were sensitized to crystallized bovine serum albumin. The mesenteric and popliteal lymph nodes were removed 3 weeks later while antibody production was relatively low. Cell suspensions from these nodes were x-radiated in vitro. The total number of cells, the viability of the cells, and the cellular differential counts were determined for the suspensions before and after radiation. The irradiated cells were injected into the abdominal wall of

immunized normal or irradiated rabbits simultaneously with the intravenous injection of radioactive iodine-tagged bovine serum albumin. The rate of elimination of labeled antigen from the blood was studied and serum antibody titers were measured after 3 to 4 days.

When nonradiated control cells were injected into irradiated recipients the antibody production was such as to cause the elimination of tagged antigen within 5 to 6 days, and circulating antibody was detected 3 to 4 days later. Irradiation of the transferred cells with 100 or 200 r caused an additional delay of 1 or 2 days in antigen elimination, and the circulating antibody levels were depressed markedly. Cells irradiated with 400 to 500 r administered to hosts treated with 400 r whole body x-radiation were incapable of producing antibody.

The injection of irradiated antibody-producing cells into nonirradiated recipients had the effect of slowing down antibody production by 1 or 2 days as compared with transferred nonirradiated cells. There was little difference in the levels of circulating antibody produced by transferred control and irradiated cells. Possibly the irradiated cells were able to recover in their nonirradiated environment. The responses of the irradiated host to transferred cells are discussed. Morphologic study of the irradiated cells showed no changes for 1 to 2 hours after irradiation. When 200 r or more was used, small lymphocytes diminished appreciably and large lymphocytes and monocytes or macrophages increased, possibly because of fluid absorption by the injured cells. These morphologic changes were not associated with alteration of immunologic function, since the cells were capable of inducing antibody formation after transfer to normal recipients.

It is concluded that both direct radiation injury to antibody-producing lymphoid tissue and irradiation damage to the host are necessary to produce significant inhibition of the secondary antibody response produced by transferred lymphoid cells. E. K.

Ethanol Fractionation of Plasma and Electrophoretic Identification of Insulin-Binding Antibody. Berson, S. A., and Yalow, R. S.: J. Clin. Invest. **36**: 642, 1957.

Nine insulin-treated, nonresistant diabetics served as serum donors. Ethanol fractionation of their sera was carried out in combination with paper electrophoresis. Insulin labeled with I^{131} was added in vitro either to the serum before fractionation or to the various fractions after separation. Antibodies were found to pure pork insulin and to pure beef insulin. Antibodies were found in fraction I plus III (beta and alpha globulins). The antibody insulin complex moved in the intergamma-beta region. The addition of insulin I^{131} did not make any detectable difference in antibody recovery in specific fractions.
E. K.

Physical Binding of Insulin by Gamma Globulins of Insulin-Resistant Subjects. Burrows, B. A., Peters, T., and Lowell, F. C., with the technical assistance of Trakas, A. N., and Reilly, P.: J. Clin. Invest. **36**: 393, 1957.

Bovine insulin labeled with I^{131} was added in vitro to serum obtained from normal individuals, treated diabetics, insulin-resistant patients, and to one insulin-resistant rabbit. A paper electrophoretic technique combined with exposure to x-ray film was employed. The sera of insulin-resistant subjects fixed the labeled insulin at the leading edge of the gamma globulin fraction. The binding activity of insulin-resistant sera ranged from 0.5 μg to over 20 μg per milliliter. The addition of human insulin to the preparation did not interfere

with the binding of labeled bovine insulin. Normal serum and nonresistant beef and pork insulin-treated diabetic serum did not bind labeled bovine insulin. It was concluded that "insulin resistance was due to the presence of antibodies which bound insulin into an inactive but soluble complex." E. K.

The Retention of S^{35}-Labelled Bovine Serum Albumin in Normal and Immunized Rabbit Liver Tissue. Garvey, J. S., and Campbell, D. H.: J. Exper. Med. **105**: 361, 1957.

Bovine serum albumin labeled with S^{35} was found to retain its label after storage in liver tissue of living rabbits. Labeled antigen was recovered from crushed liver tissue by a new method which is described in detail. The amount of antigen "retained in liver tissue 1 day after a single injection . . . was about 7.0 per cent of the total amount injected (as based on radioactivity)." Thereafter, the amount retained slowly decreased. This purified material formed with specific antibody a precipitate in which all of the radioactivity was contained. The retained antigen was capable of sensitizing guinea pigs actively, less of the retained antigen being required than original antigen for this purpose. Bovine serum albumin was still present in liver tissue of rabbits 140 days after injection. The rate of disappearance of antigen was so slow that "significant amounts would be expected to persist for at least several years." S^{35}-labeled hemocyanin antigen could be detected 330 days after injection.
E. K.

Antigenicity of Egg White Proteins in the White Mouse. Malkiel, S.: Proc. Soc. Exper. Biol. & Med. **95**: 133, 1957.

It has been shown by various workers that in "specific" antisera directed against crystalline ovalbumin antibodies for conalbumin, ovomucoid, lysozyme, and other antigenic impurities are found. The sensitizing capacities and antigenic relationship of these contaminants of crystalline ovalbumin were studied in white mice with the pertussis technique (Malkiel and Hargis). Female white mice (Swiss-Webster strain) were sensitized by an intraperitoneal injection of egg white in a suspension of *H. pertussis* phase I organisms. After ten days the mice were challenged intravenously with homologous or heterologous antigens of egg white.

In the pertussis-treated mice conalbumin and lysozyme proved to be effective antigens. In mice sensitized to ovalbumin, conalbumin proved to be antigenic but lysozyme was not. However, ovalbumin was able to shock mice sensitized to conalbumin and lysozyme. Ovomucoid was not capable of sensitizing white mice with this technique. B. S.

Miscellaneous

Anesthetic Management of Patients With Respiratory Disease. Greene, N. M.: J. A. M. A. **162**: 1276, 1956.

Respiratory disease in a surgical patient represents a serious complication to the administration of anesthesia. Preoperative management necessitates the control of respiratory infection and adequate allergic treatment of asthmatics who may require, in addition, bronchodilator drugs and steroid therapy. Patients with severe pulmonary emphysema who demonstrate carbon dioxide retention and respiratory acidosis are given acetazolamide (Diamox) in doses of 250 to 750 mg. per day for 4 to 5 days. This drug produces a bicarbonate diuresis which leads to a reduction of carbon dioxide tension in the blood plasma, resulting in a reduced carbon dioxide tension in the alveoli. The metabolic acidosis

which results is corrected on the day prior to surgery, when the drug is replaced by ammonium chloride. For preanesthetic medication, hypnotic doses of barbiturates are preferable to narcotics, since the latter produce respiratory depression while the former do not.

It is stressed that none of the presently available anesthetic agents or techniques is ideal, that anesthetic agents per se have no influence on the incidence of postoperative respiratory complications, and finally that, although preexisting pulmonary infections are adversely affected by anesthesia and surgery, the degree to which they are influenced is not related to the particular type of general anesthetic used.

Ether, the most potent inhalation anesthetic commonly used today, can be administered with a higher concentration of oxygen than can be used with any other agent. Surgical anesthesia with muscular relaxation is maintained with 4 per cent ether and 96 per cent oxygen in the inspired air. Ether is also the only general anesthetic that does not invariably cause depression of respiration to the point where respiratory acidosis supervenes. Alveolar respiration may actively increase except in deeper planes of anesthesia. Respiratory acidosis occurs, but it is neither as frequent nor as severe as that present with other agents. In asthma, ether is preferable to all other general anesthetic agents. With the single exception of tribromoethanol (Avertin), ether is the only agent possessing bronchodilator properties. The major disadvantage of ether is that recovery may be prolonged. However, recovery is not accompanied by the same respiratory depression that follows recovery from equal depths of anesthesia produced by other general anesthetics.

Cyclopropane is administered with high concentrations of oxygen but, unlike ether, it produces depression of the respiratory center and respiratory acidosis. All patients must have their respirations assisted or controlled during cyclopropane anesthesia. Its greatest advantage lies in the ready reversibility of the anesthesia induced. It is a good anesthetic in patients with respiratory disease, except in asthmatics because of its tendency to produce bronchospasm.

Anesthesia with intravenously given barbiturates is often not desirable in patients with respiratory disease, since respiratory depression results and the action of the drugs is not rapidly and readily reversible. Muscle relaxant drugs are dangerous in that the muscles of respiration are impaired and the duration of action of these agents may extend into the postoperative period. Spinal anesthesia is eminently satisfactory for patients with respiratory disease during major surgery performed below the umbilicus. High spinal anesthesia is contraindicated, however. Competent postoperative care is centered on the prevention or correction of any interference with adequate respiration and completes the program of providing safe anesthesia for patients with respiratory disease. M. C.

The Distribution of CR^{51} Labeled E. Coli Endotoxin in the Generalized Shwartzman Reaction. Smith, R. T., Braude, A. I., and Carey, F. J.: J. Clin. Invest. **36**: 695, 1957.

Rabbits were given an intravenous injection of unlabeled *E. coli* endotoxin. After 24 hours, these and normal rabbits were injected intravenously with *E. coli* endotoxin labeled with $Cr^{51}Cl_3$. Autopsies were then performed at various time intervals. In the endotoxin-prepared rabbits there was striking reduction in concentration of radioactivity in the liver and an increased radioactivity in the lungs. In animals developing bilateral renal cortical necrosis, radioconcentration was also excessive in the kidney. It is suggested that the trapping of leukocytes containing radioactive endotoxin may account for the concentration of radioactivity in the kidney and lung. Impairment of liver uptake by the

preparatory toxin injection is consistent with the observation that other effective Shwartzman preparatory techniques consist of blockade of the reticuloendothelial system. E. K.

A Possible Source of Bacterial Contaminants in Transfused Blood. Rosenzweig, A. L.: Am. J. Clin. Path. **27**: 639, 1957.

The adequacy of rubber stoppers on 100 vacuum bottles was studied by piercing them with 15- and 17-gauge needles and then flooding the tops with methylene blue solution. Twenty per cent of the bottles showed seepage of dye into the bottle. Introduction of the needle at an angle facilitated seepage of dye into the bottle. No leak of air was observable on the leaking bottles. That bacteria could seep through the needle path was also demonstrated with cultures of *Pseudomonas* and *E. coli.* Of 16 bottles tested, 4 showed growth of these contaminants. Eight control bottles sealed with nail polish remained sterile. It is concluded that rubber stoppers on blood donor bottles are not completely self-sealing. Suggestions made to control this hazard include the use of an antiseptic after puncture, followed by a coating of colorless nail polish or copal varnish (dental cavity lining). E. K.

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American Academy of Allergy, Fourteenth Annual Meeting
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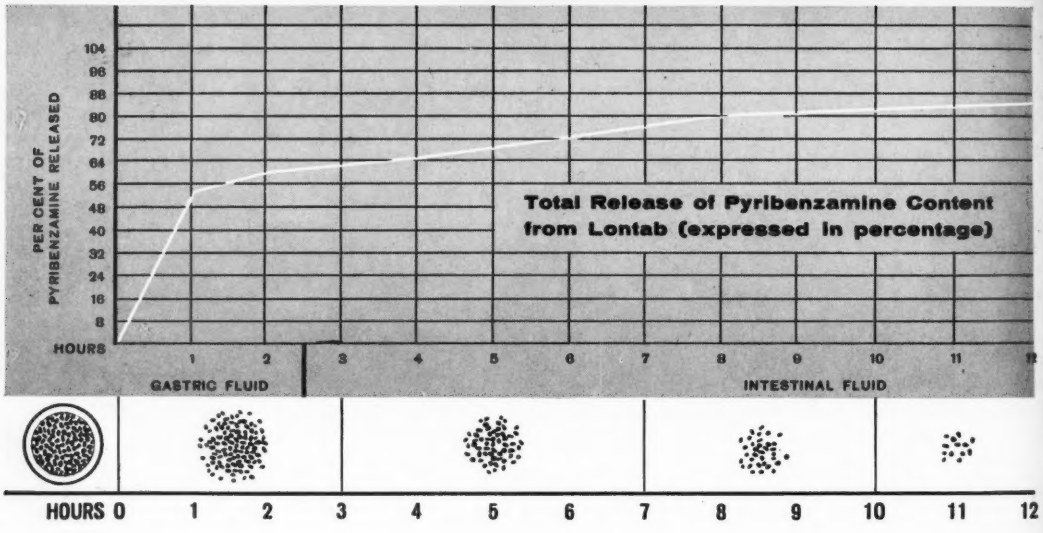

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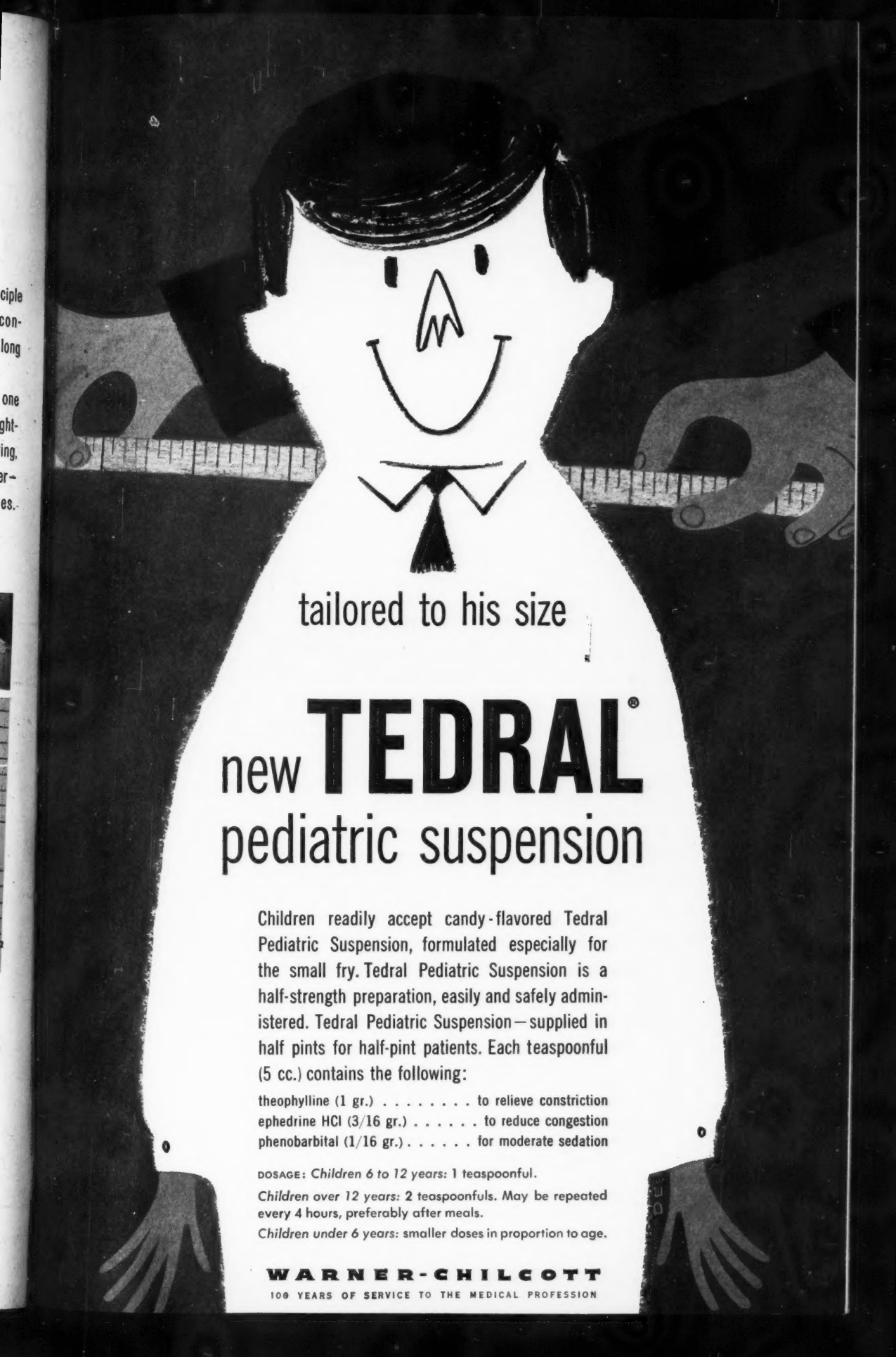
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Vol. 28, No. 6, November, 1957. The Journal of Allergy is published bi-monthly by The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo. Subscription rates: United States and its Possessions $8.50, Students $4.25; Canada, Latin-America, and Spain $9.00, Students $4.75; Other Countries $9.50, Students $5.25. Single copies $2.50 postpaid. Entered as Second-Class Matter, November 15, 1929, at the Post Office at St. Louis, Missouri, under the Act of March 3, 1879. Printed in the U. S. A.

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Published Bimonthly. Subscriptions may begin at any time.

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Original Communications.—Manuscripts for publication, letters, and all other communications relating to the editorial management of the Journal should be sent to the editor, Francis C. Lowell, M.D., 65 E. Newton St., Boston, Mass. Articles are accepted for publication upon the understanding that they are contributed solely to THE JOURNAL OF ALLERGY.

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Publication Order.—This Journal is published bimonthly, January through November. The volume index is in the November issue.

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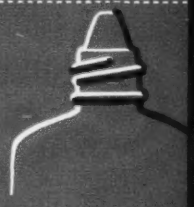

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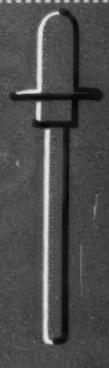

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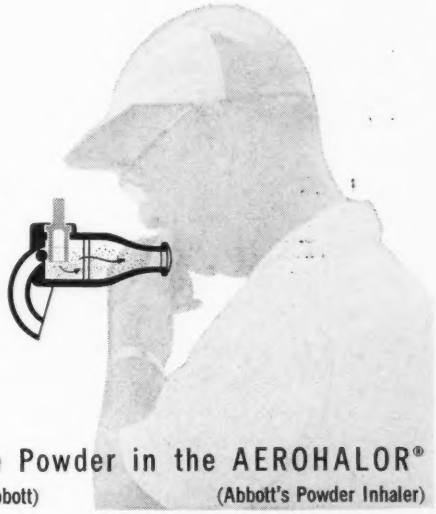

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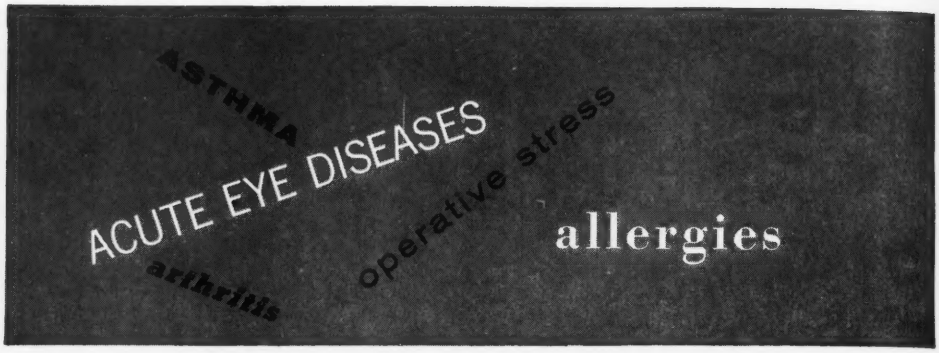

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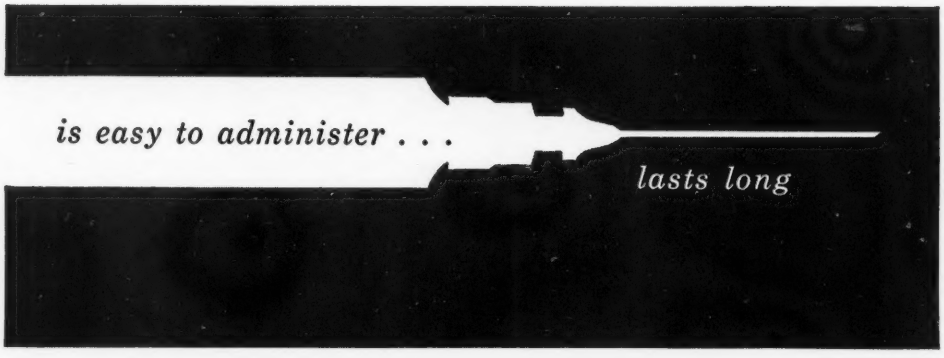

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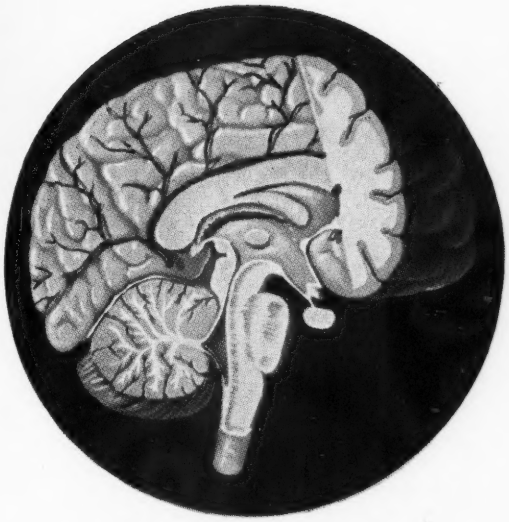

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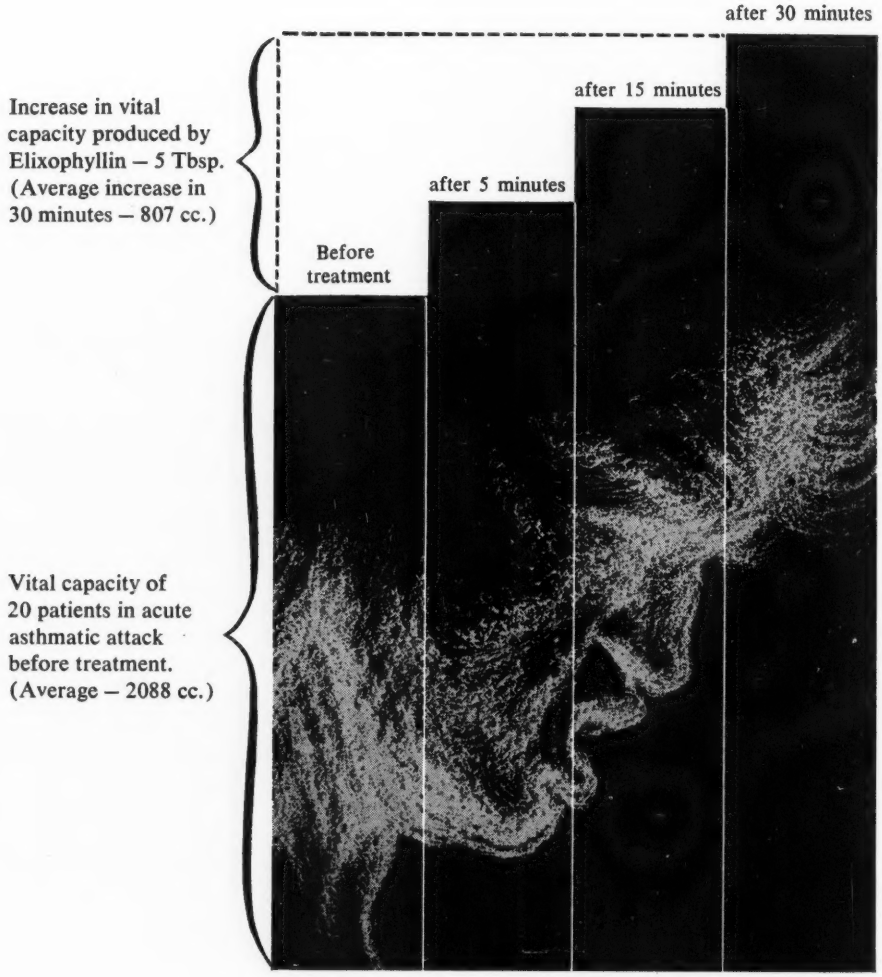
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1. Schluger, J., et. al.: Am. J. M. Sci. 233:296, 1957.
2. Spielman, D.: Ann. Allergy (in press).
3. Kessler, F.: Connecticut St. M.J. 21:205, 1957.
4. Schluger, J., et al.: Am. J. M. Sci. (in press).
5. Greenbaum, J.: (to be published).
6. Waxler, S. J. & Schack, J. A.: J. A. M. A. 143:736, 1950.
7. Bradwell, E. K.: Acta med. scandinav. 146:123, 1953.

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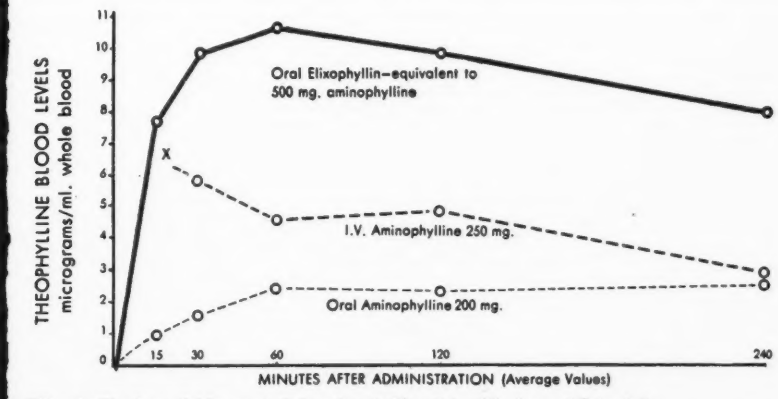

Elixophyllin data—Schluger et al.;[1] aminophylline data—Waxler and Schack.[6]
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Allergic dermatitis	2		1	1		Slight Drowsiness (2)
Bronchial asthma	1		1			
Pruritus	1		1			
Total	37	15	13	7	2	Drowsiness (5) Dizzy (1) 16.2%

From the preliminary Dimetane Extentabs studies of three investigators. Further clinical investigations will be reported as completed.

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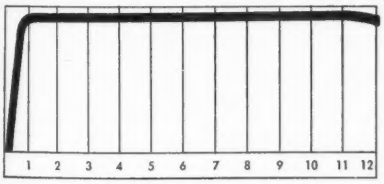

Dosage:

Adults—One or two 4-mg. tabs. or two to four teaspoonfuls Elixir, three or four times daily. One Extentab q.8-12h. or twice daily. Children over 6—One tab. or two teaspoonfuls Elixir t.i.d. or q.i.d., or one Extentab q.12h. Children 3-6—½ tab. or one teaspoonful Elixir t.i.d.

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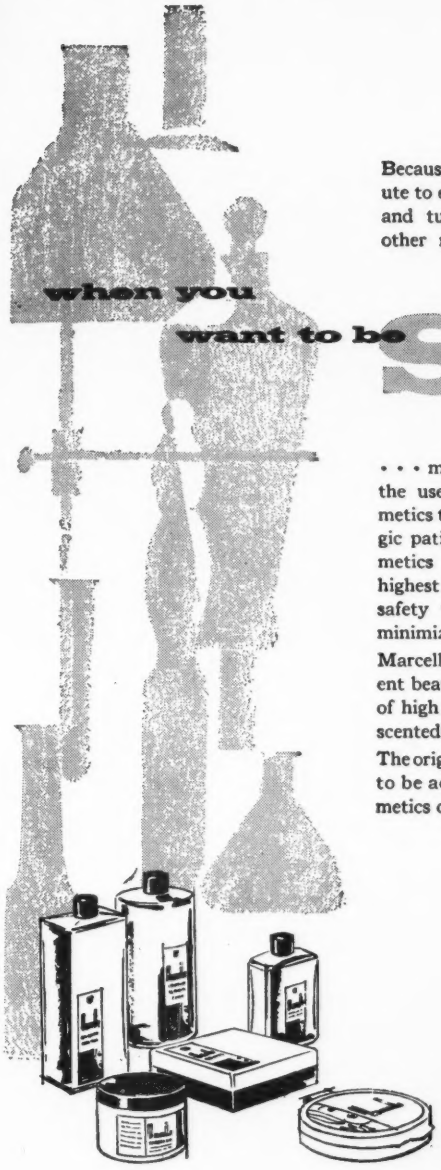
*Silbert, N. E., Ciba Clinical Symposia; 6: 86; May 1954
Mechaneck, I., Annals of Allergy; 12: 164: March 1954
Rosen, F. L., J. Med. Soc. N. J.: 51: 110: March 1954
Mueller, H. L., & Hill, L. W.: N. E. J. of Med; 249: 726, 1953



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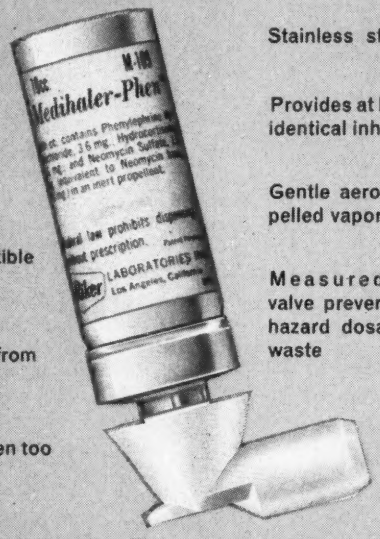

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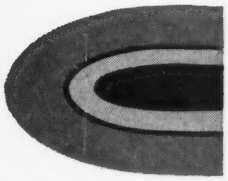

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1. Spielman, A. D.: Personal communication. 2. New and Unused Therapeutics Committee, Am. Coll. Allergists: Interim Report at Thirteenth Annual Congress, Mar. 20-22, 1957, Chicago, Ill., Ann. Allergy, to be published.

5773

Occupational Diseases of the Skin

By LOUIS SCHWARTZ, M.D.
Medical Director (Retired), United States Public Health Service, Chief, Dermatoses Section; Consultant in Dermatology, National Institutes of Health; Consultant in Dermatology, USPHS

LOUIS TULIPAN, M.D.
Emeritus Clinical Professor of Dermatology, New York University, Bellevue Post-Graduate Medical School; Consulting Dermatologist, Bellevue Hospital, New York City

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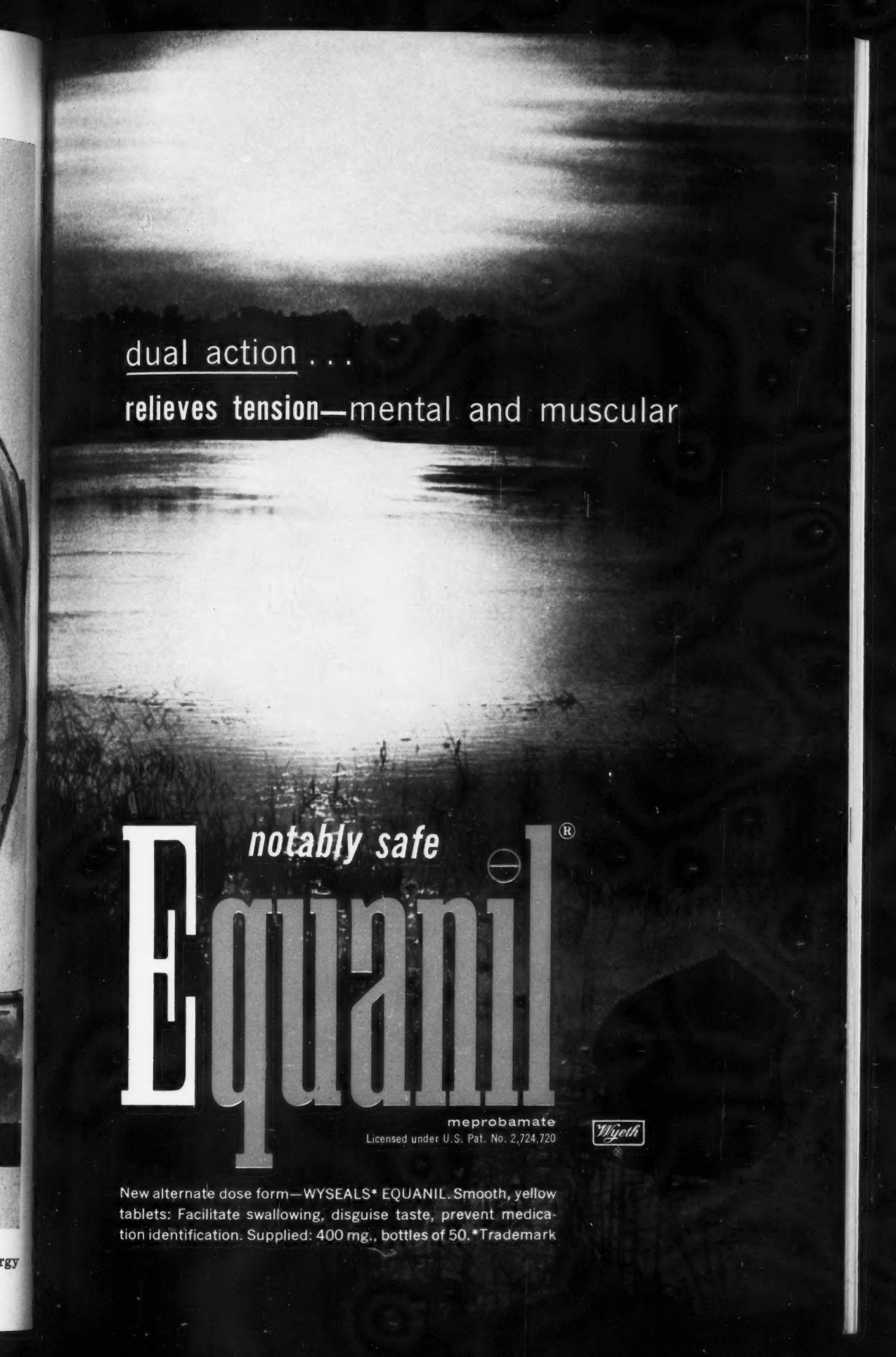
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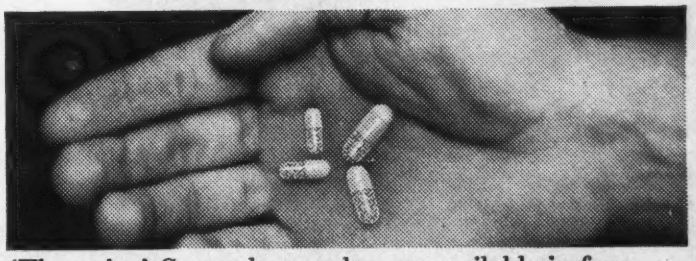

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1. Brown, E. A., and Clancy, R. E.: Ann. Allergy *13*:543, 1955.
2. J.A.M.A. *160*:467, 1956.

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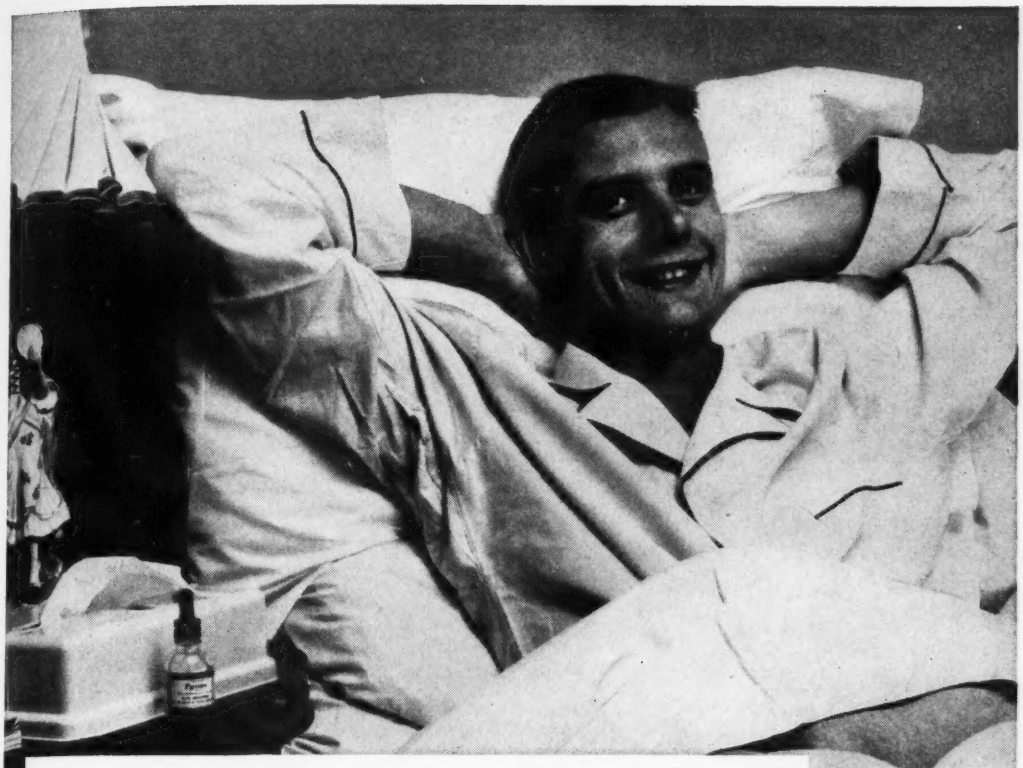

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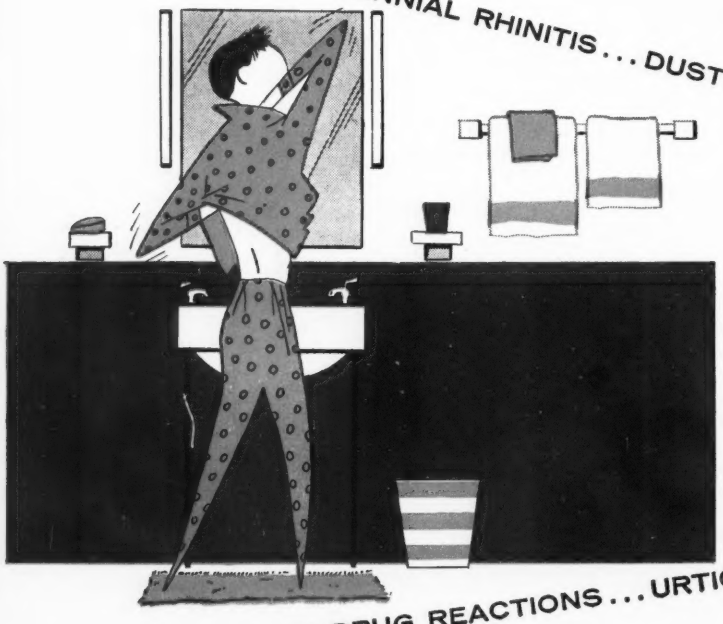

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1. Johnson, H. J., Jr.: Clinical Evaluation of a New Antihistaminic: Clistin Maleate, Amer. Pract. & Digest. Treat. *5*:862 (Nov.) 1954.
2. Council on Pharmacy & Chemistry: New and Non-official Remedies, 1957, Philadelphia, J. B. Lippincott Co., 1957, p. 8.
3. Beale, H. D., et al.: Clistin Maleate. A Clinical Appraisal of a New Antihistaminic, J. Allergy *25*:521 (Nov.) 1954.

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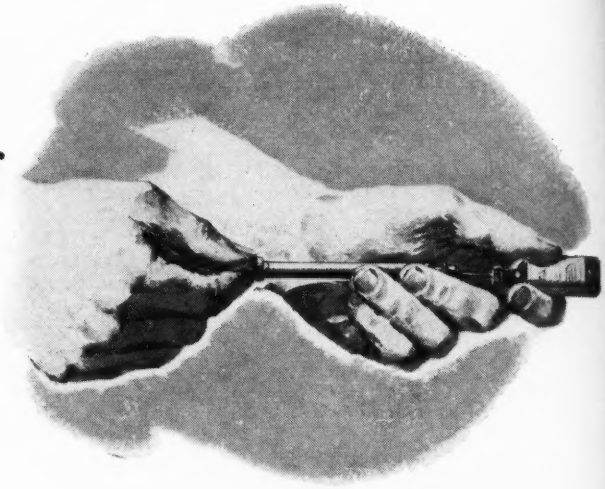

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1. Levin, S.: J. Ped. Clin. of N.A., 1:975 (1954).
2. Naterman, H.L.: J. of Allergy, 20:64 (1953).
3. Unger, A.H., and Unger, L.: Ann. of Allergy, 10:128 (1952).
4. Jenkins, C.M.: J. Nat. Med. Assn., 45:120 (1953).

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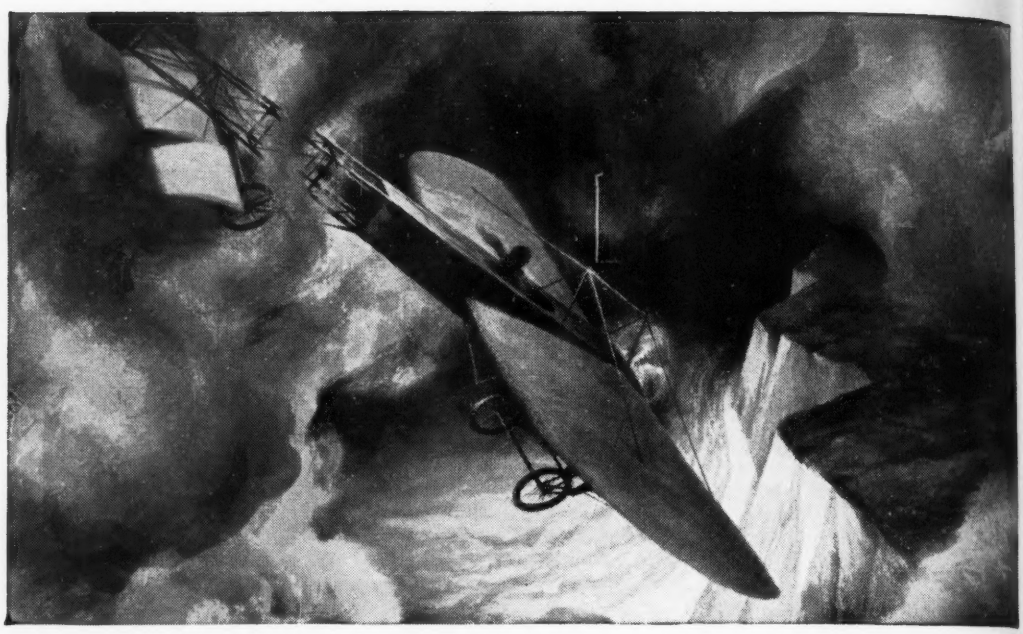

HER ENGINE FALTERED

A few minutes out of Dover, fog wrapped the flimsy Bleriot monoplane like a shroud.

The pretty young woman in the smart flying costume (she'd designed it herself—"bloomers, blouse, and hood of mauve satin") glanced at her compass. It was the first time she'd ever used one. She thought of instructor Hamel's parting words:

"Be sure to keep on course, Miss Quimby, for if you get five miles out of the way, you'll be over the North Sea, and you know what that means."

She climbed to 6,000 feet. Freezing cold and still fog.

She pointed her nose down. The comforting clatter of the Gnome engine changed to a coughing splutter. It was conking out! She leveled off, figuring how she'd ditch. To her relief, the engine suddenly took hold. Harriet re-checked her compass.

Some time later, breaking into clear sky, she saw a stretch of beach below. She put down at Hardelot; and on April 16, 1912, Harriet Quimby, first American woman to earn a pilot's license, became the first woman in the world to fly the English Channel.

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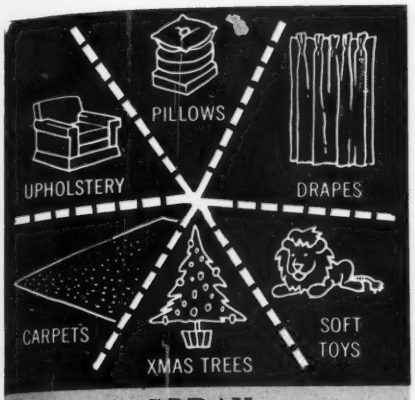

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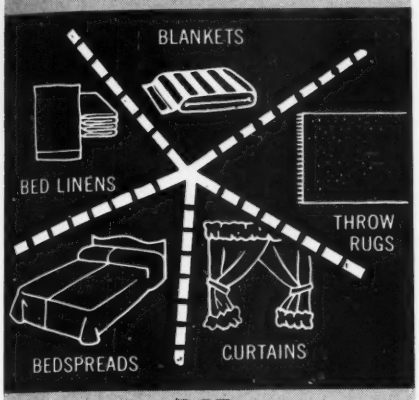

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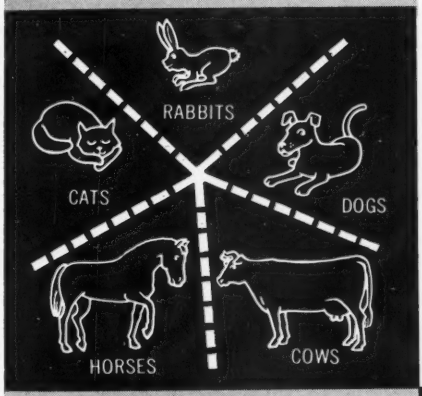

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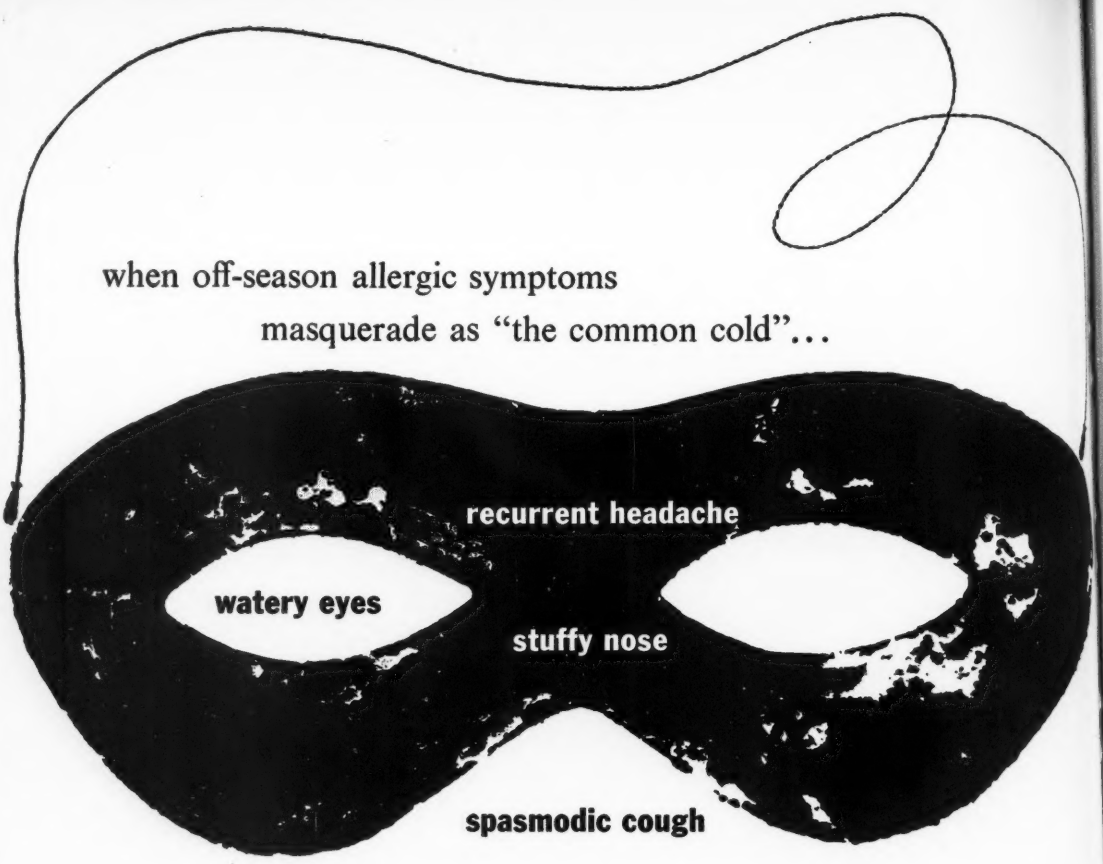

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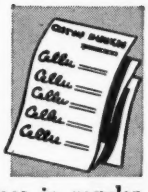

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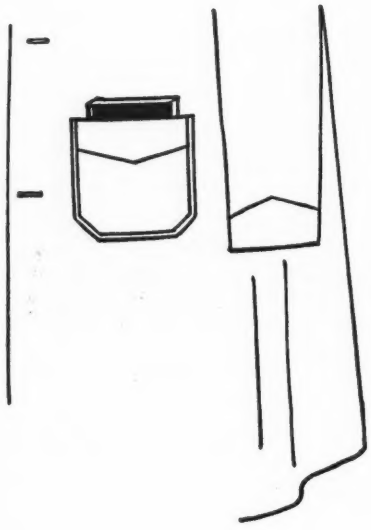

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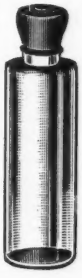

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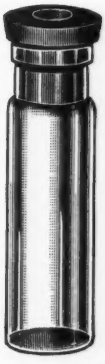

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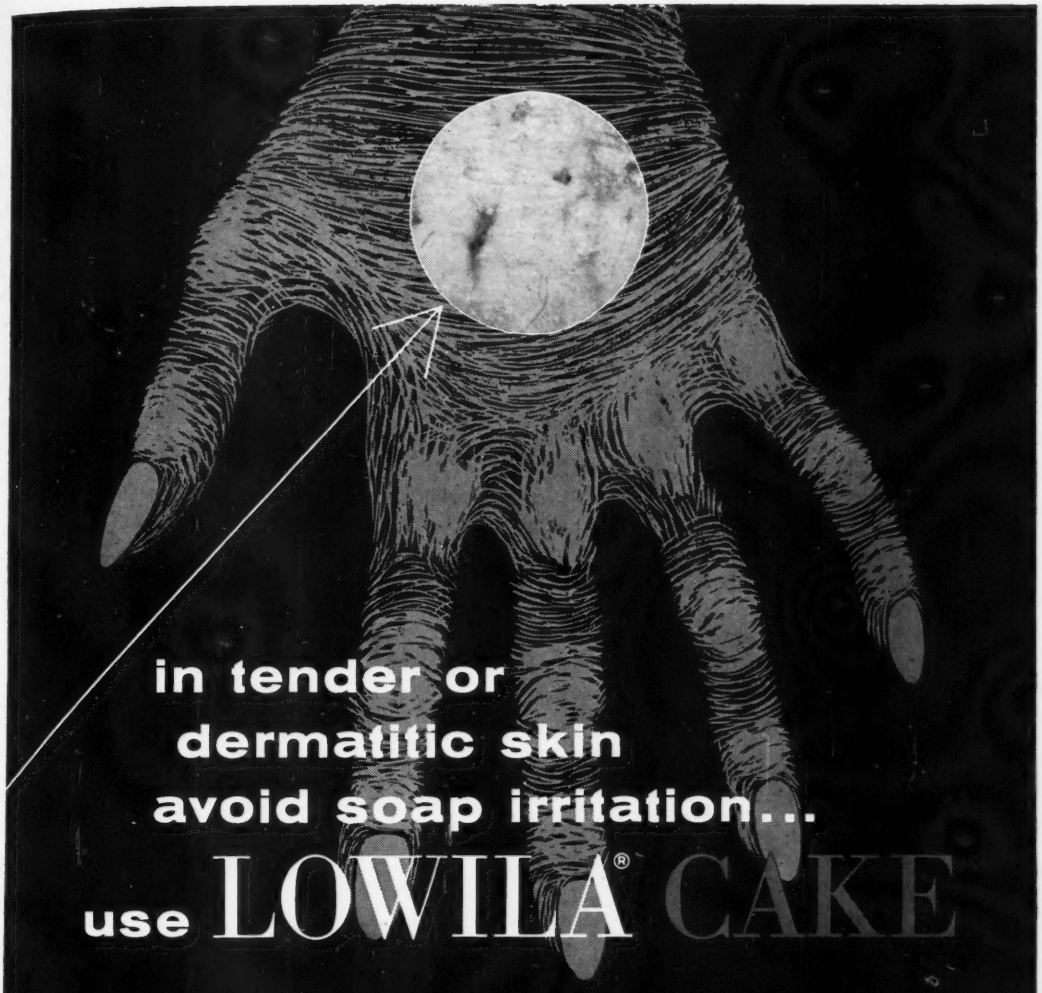

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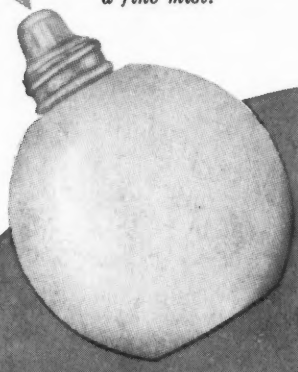

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Neo-Synephrine (brand of phenylephrine) and Thenfadil (brand of thenyldiamine), trademarks reg U.S. Pat. Off.

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